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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 00-713-i16)

PATENT

Application of:

Chad A. Mirkin, et al.

Serial No.: 09/976,601

Filed: October 12, 2001

For: NANOPARTICLES HAVING
OLIGONUCLEOTIDES ATTACHED
THERE TO AND USES THEREFOR

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Examiner: J. Riley

Art Unit: 1656

Confirmation No. 4367

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TRANSMITTAL LETTER

Commissioner for Patents and Trademarks
Washington, D.C. 20231

Sir:

In regard to the above identified application.

1. We are transmitting herewith the attached:

- a) Information Disclosure Statement copies of 16 references
- b) Supplemental Information Disclosure Statement with copies of 9 references
- c) Second Supplemental Information Disclosure Statement with copies of 3 references
- d) Third Supplemental Information Disclosure Statement with copies of 5 references
- e) Fourth Supplemental Information Disclosure Statement with copies of 60 references
- f) Fifth Supplemental Information Disclosure Statement with copies of 4 references
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2. With respect to fees:

- a) No check is attached.
- b) General Authorization: Please charge any underpayment or credit any overpayment our Deposit Account, No. 13-2490.

3. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1 hereinabove, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Commissioner for Patents and Trademarks, Washington, D.C. 20231 on this 31 day of January, 2002.

Date:

1/31/02

Respectfully submitted,

Emily Miao
Registration No. 35,285

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INFORMATION DISCLOSURE STATEMENT

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Sir:

In order to comply with discretionary regulations 37 CFR §§1.97 and 1.98, attached hereto is Form PTO-1449, copies¹ of the documents listed thereon. These documents contain information which the Examiner may consider to be important in deciding whether to allow the present application to issue as a patent.

1. Mroczkowski, et al., U.S. Patent No. 5,284,748, issued 02/08/94.
2. Engelhardt, et al., U.S. Patent No. 5,288,609, issued 02/22/94.
3. Hainfield, et al., U.S. Patent No. 5,360,895, issued 11/01/94.
4. Kidwell, et al., U.S. Patent No. 5,384,265, issued 01/24/95.

¹To the extent that a document is listed and no copy of same is attached, then such document is not at the present time available to the undersigned or is available in the file of a parent application. If a listed document is not in the English language and an English translation is readily available, such translation is also attached; if translation is not attached it is not readily available to the undersigned. If a foreign language patent document is cited, and an English language equivalent is known to the undersigned, then such equivalent patent is also cited on the attached form along with the corresponding foreign language patent and a connecting arrow indicated therebetween; if no such English language equivalent is cited, then none is known to undersigned.

5. Beebe, et al., U.S. Patent No. 5,472,881, issued 12/05/95.
6. Stimpson, et al., U.S. Patent No. 5,599,668, issued 02/04/97.
7. Kidwell, et al., U.S. Patent No. 5,637,508, issued 06/10/97.
8. Alivisatos, et al., U.S. Patent No. 5,751,018, issued 05/12/98.
9. Hansen, et al., U.S. Patent No. 5,939,021, issued 08/17/99.
10. Weiss, et al., U.S. Patent No. 5,990,479, issued 11/23/99.
11. WO 93/10564 published 27 May 1993.
12. WO 98/10289 published 12 March 1998.
13. WO 99/23258 published 14 May 1999.
14. WO 99/21934 published 06 May 1999.
15. WO 99/20789 published 29 April 1999.
16. O.D. Velez, et al., "In Situ Assembly of Colloidal Particles into Miniaturized Biosensors," *Langmuir*, May 25, 1999, Vol. 15, No. 11, pp. 3693-3698 (May 25, 1999)

In accordance with MPEP Sections 609 and 707.05(b), it is requested that each document cited (including any cited in applicant's specification which is not repeated on the attached Form PTO-1449) be given thorough consideration and that it be cited of record in the prosecution history of the present application by initialing on Form PTO-1449. Such initialing is requested even if the Examiner does not consider a cited document to be sufficiently pertinent to use in a rejection, or otherwise does not consider it to be prior art for any reason, or even if the Examiner does not believe that the guidelines for citation have been fully complied with. This is requested so that each document becomes listed on the face of the patent issuing on the present application.

The present Disclosure Statement is being submitted in compliance with 37 CFR 1.56 insofar as an Examiner might consider any of the cited documents important in deciding whether to

allow the application to issue as a patent, but the citation of each document is not to be construed as an admission that such document is necessarily relevant or prior art. No representation is intended that the cited documents represent the results of a complete search, and it is anticipated that the Examiner, in the normal course of examination, will make an independent search and will determine the best prior art consistent with 37 CFR 1.104(a) and 1.106(b) and, in the course of each search, will review for relevance every document cited on the attached form even if not initialed.

Early and favorable consideration is earnestly solicited.

Respectfully submitted,



Emily Miao
Registration No. 35,285

Dated: _____

1/31/02

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 00-713-i16)

In the Application of:

Chad A. Mirkin, et al.

Serial No.: 09/976,601

Filed: October 12, 2001

For: NANOPARTICLES HAVING
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) Examiner: Jezia Riley
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) Group Art Unit: 1656
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Washington, D.C. 20231

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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

In order to comply with discretionary regulations 37 CFR §§1.97 and 1.98, attached hereto is Form PTO-1449, copies¹ of the documents listed thereon. These documents contain information which the Examiner may consider to be important in deciding whether to allow the present application to issue as a patent.

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3. Stimpson, et al., "Real-time detection of DNA hybridization and melting on oligonucleotide arrays by using optical wave guides," *Proc. Natl. Acad. Sci.*, Vol. 92, pp. 6379-6383, California Institute of Technology (1995) U.S.
4. Storhoff, et al., "Strategies for Organizing Nanoparticles into Aggregate Structures and Functional Materials," *Journal of Cluster Science*, Vol. 8, No. 2, pp. 179-217, Plenum Publishing Corporation (1997) U.S.
5. Storhoff, et al., "One-Pot Colorimetric Differentiation of Polynucleotides with Single Base Imperfections Using Gold Nanoparticle Probes," *J. Am. Chem. Soc.*, Vol. 116, pp. 1959-1964, American Chemical Society (1994) U.S.
6. Velev, et al., "In Situ Assembly of Colloidal Particles into Miniaturized Biosensors," *Langmuir*, Vol. 15, No. 11, pp. 3693-3698, American Chemical Society (1999) U.S.
7. Zhu, et al., "The First Raman Spectrum of an Organic Monolayer on a High-Temperature Superconductor: Direct Spectroscopic Evidence for a Chemical Interaction between an Amine and $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}$," *J. Am. Chem. Soc.*, Vol. 119, pp. 235-236, American Chemical Society (1997) U.S.
8. Yguerabide, et al., "Light-Scattering Submicroscopic Particles as Highly Fluorescent Analogs and Their Use as Tracer Labels in Clinical and Biological Applications," I. Theory, *Analytical Biochemistry*, Vol. 262, pp. 137-156 (1998) U.S.
9. Yguerabide, et al., "Light-Scattering Submicroscopic Particles as Highly Fluorescent Analogs and Their Use as Tracer Labels in Clinical and Biological Applications," II. Experimental Characterization, *Analytical Biochemistry*, Vol. 262, pp. 157-176 (1998) U.S.

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Dated: _____

1/31/02

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Respectfully submitted,



Emily Miao
Registration No. 35,285



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 00-713-116)

In the Application of:

Chad A. Mirkin, et al.

Serial No.: 09/976,601

Filed: October 12, 2001

For: NANOPARTICLES HAVING
OLIGONUCLEOTIDES ATTACHED
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) Examiner: Jezia Riley
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) Group Art Unit: 1656
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) Confirmation No. 4367
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Washington, D.C. 20231

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SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

In order to comply with discretionary regulations 37 CFR §§1.97 and 1.98, attached hereto is Form PTO-1449, copies¹ of the documents listed thereon. These documents contain information which the Examiner may consider to be important in deciding whether to allow the present application to issue as a patent.

1. Natan, U.S. Patent No. 5,609,907, issued March 11, 1997.
2. Natan, U.S. Patent No. 6,025,202, issued February 15, 2000.
3. Natan, et al., U.S. Patent No. 6,149,868, issued November 21, 2000.

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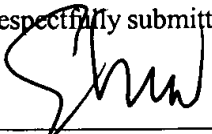
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Early and favorable consideration is earnestly solicited.

Dated: 1/31/02

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Respectfully submitted,



Emily Miao
Registration No. 35,285



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 00-713-i16)

the Application of:)
Chad A. Mirkin, et al.)
Serial No.: 09/976,601) Examiner: Jezia Riley
Filed: October 12, 2001) Group Art Unit: 1656
For: NANOPARTICLES HAVING) Confirmation No. 4367
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THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

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1. Brada, et al., "Golden Blot" – Detection of Polyclonal and Monoclonal Antibodies Bound to Antigens on Nitrocellulose by Protein A-Gold Complexes, *Analytical Biochemistry*, Vol. 42, pp. 79-83 (1984) U.S.

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2. Dunn, et al., "A Novel Method to Map Transcripts: Evidence for homology between an Adenovirus mRNA and Discrete Multiple Regions of the Viral Genome, *Cell*, Vol. 12, pp. 23-36, (1997) U.S.
3. Hacker, "High performance Nanogold – Silver in situ hybridisation, *Eur. J. Histochem*, Vol. 42, pp. 111-120 (1998) U.S.
4. Ranki, et al., "Sandwich hybridization as a convenient method for the detection of nucleic acids in crude samples," *Gene*, Vol. 21, pp. 77-85 (1983) U.S.
5. Romano, et al., "An antiglobulin reagent labelled with colloidal gold for use in electron microscopy," *Immunochemistry*, Vol. 11, pp. 521-522 (1974) Great Britain

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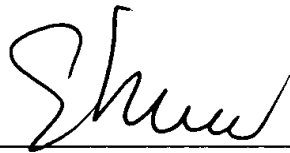
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Emily Miao
Registration No. 35,285

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In the Application of:

Chad A. Mirkin, et al.

Serial No.: 09/976,601

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FOURTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

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1. Ullman et al., U.S. Patent No. 4,193,983 issued 03/18/80
2. Zuk et al., U.S. Patent No. 4,256,834 issued 03/17/81
3. Ullman et al., U.S. Patent No. 4,261,968 issued 04/14/81
4. Leuving, U.S. Patent No. 4,313,734 issued 02/02/82
5. Litman et al., U.S. Patent No. 4,318,707 issued 03/09/82

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6. Liu et al., U.S. Patent No. 4,650,770 issued 03/17/87
7. Ullman, U.S. Patent No. 4,713,348 issued 12/15/87
8. Olsen et al., U.S. Patent No. 4,853,335 issued 08/01/89
9. Kura et al., U.S. Patent No. 4,868,104 issued 09/19/89
10. Henkens et al., U.S. Patent No. 5,225,064 issued 07/06/93
11. Shigekawa et al., U.S. Patent No. 5,294,369 issued 03/15/94
12. Shigekawa et al., U.S. Patent No. 5,384,073 issued 01/24/95
13. Kidwell et al., U.S. Patent No. 5,384,265 issued 01/24/95
14. Kossovsky et al., U.S. Patent No. 5,460,831 issued 10/24/95
15. Beebe et al., U.S. Patent No. 5,472,881 issued 12/05/95
16. Brooks, Jr. et al., U.S. Patent No. 5,514,602 issued 05/07/96
17. Hainfeld et al., U.S. Patent No. 5,521,289 issued 05/28/96
18. Gref et al., U.S. Patent No. 5,543,158 issued 08/06/96
19. Brooks, Jr. et al., U.S. Patent No. 5,571,726 issued 11/05/96
20. Kaushch et al., U.S. Patent No. 5,665,582 issued 09/09/97
21. Letsinger et al., U.S. Patent No. 5,681,943 issued 10/28/97
22. International Patent No. WO 89/06801 published 07/27/89
23. International Patent No. WO 97/40181 published 10/30/97
24. International Patent No. WO 98/04740 published 02/05/98
25. International Patent No. WO 99/23258 published 05/14/99
26. European Patent 0 630 974 A2 published 06/21/94
27. European Patent 0 667 398 A2 published 08/16/95
28. Alivisatos et al., "Organization of 'nanocrystal molecules' using DNA," *Nature*, Vol. 382, pp. 609-611 (1996)

29. Bain, et al., "Modeling Organic Surfaces with Self-Assembled Monolayers," *Angew. Chem. Int. Ed. Engl.*, Vol. 28, pp. 506-512 (1989)
30. Bradley, "The Chemistry of Transition Metal Colloids," *Clusters and Colloids: From Theory to Applications*, G. Schmid, Editor, BCH, Weinheim, New York, pp. 459-542 (1994)
31. Brust et al., "Novel Gold-Dithiol Nano-Networks with Non-Metallic Electronic Properties," *Adv. Mater.*, Vol. 7, pp. 795-797 (1995)
32. Chen et al., "A Specific Quadrilateral Synthesized from DNA Branched Junctions," *J. Am. Chem. Soc.*, Vol. 111, pp. 6402-6407 (1989)
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34. Chen et al., "Crystal Structure of a Four-Stranded Intercalated DNA: d(C₄)^{††} *Biochem.*, Vol. 33, pp. 13540-13546 (1994)
35. Dagani, "Supramolecular Assemblies DNA to organize gold nanoparticles," *Chemical & Engineering News*, p. 6-7, August 19, 1996
36. Dubois & Nuzzo, "Synthesis, Structure, and Properties of Model Organic Surfaces," *Annu. Rev. Phys. Chem.*, Vol. 43, pp. 437-464 (1992)
37. Elghanian et al., "Selective Colorimetric Detection of Polynucleotides Based on the Distance-Dependent Optical Properties of Gold Nanoparticles," *Science*, Vol. 277, pp. 1078-1081 (1997)
38. Grabar et al., "Preparation and Characterization of Au Colloid Monolayers," *Anal. Chem.* Vol. 67, pp. 735-743 (1995)
39. Hacia et al., "Detection of heterozygous mutations in BRCA1 using high density oligonucleotide arrays and two-colour fluorescence analysis," *Nature Genet.*, Vol. 14, pp. 441-447 (1996)
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41. Letsinger et al., "Use of Hydrophobic Substituents in Controlling Self-Assembly of Oligonucleotides," *J. Am. Chem. Soc.*, Vol. 115, pp. 7535-7536 (1993)

42. Letsinger et al., "Control of Excimer Emission and Photochemistry of Stilbene Units by Oligonucleotide Hybridization," *J. Am. Chem. Soc.*, Vol. 116, pp. 811-812 (1994)
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44. Mirkin, "H-DNA and Related Structures," *Annu. Review Biophys. Biomol. Struct.*, Vol. 23, pp. 541-576 (1994)
45. Mirkin et al., "A DNA-based method for rationally assembling nanoparticles into macroscopic materials," *Nature*, Vol. 382, pp. 607-609 (1996)
46. Mirkin et al., "DNA-Induced Assembly of Gold Nanoparticles: A Method for Rationally Organizing Colloidal Particles into Ordered Macroscopic Materials," *Abstract 249*, Abstracts of Papers Part 1, 212 ACS National Meeting 0-8412-3402-7, American Chemical Society, Orlando, FL, August 25-29, 1996
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48. Mulvaney, "Surface Plasmon Spectroscopy of Nanosized Metal Particles," *Langmuir*, Vol. 12, pp. 788-800 (1996)
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51. Seeman et al., "Synthetic DNA knots and catenanes," *New J. Chem.*, Vol. 17, pp. 739-755 (1993)
52. Shaw & Wang, "Knotting of a DNA Chain During Ring Closure," *Science*, Vol. 260, pp. 533-536 (1993)
53. Shekhtman et al., "Stereostructure of replicative DNA catenanes from eukaryotic cells," *New J. Chem.* Vol. 17, pp. 757-763 (1993)

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55. Thein et al., "The use of synthetic oligonucleotides as specific hybridization probes in the diagnosis of genetic disorders," 2nd Ed., K.E. Davies, Ed., Oxford University Press, Oxford, New York, Tokyo, p. 21-33 (1993)
56. Wang et al., "Assembly and Characterization of Five-Arm and Six-Arm DNA Brached Junctions," *Biochem.*, Vol. 30, pp. 5667-5674 (1991)
57. Wang et al., "A DNA Aptamer Which Binds to and Inhibits Thrombin Exhibits a New Structural Motif for DNA," *Biochem.*, Vol. 32, pp. 1899-1904 (1993)
58. Weisbecker et al., "Molecular Self-Assembly of Aliphatic Thiols on Gold Colloids," *Langmuir*, Vol. 12, pp. 3763-3772 (1996)
59. Wells, "Unusual DNA Structures," *J. Biol. Chem.*, Vol. 263, pp. 1095-1098 (1988)
60. Zhang et al., "Informational Liposomes: Complexes Derived from Cholesteryl-conjugated Oligonucleotides and Liposomes," *Tetrahedron Lett.*, Vol. 37, pp. 6243-6246 (1996)

In accordance with MPEP Sections 609 and 707.05(b), it is requested that each document cited (including any cited in applicant's specification which is not repeated on the attached Form PTO-1449) be given thorough consideration and that it be cited of record in the prosecution history of the present application by initialing on Form PTO-1449. Such initialing is requested even if the Examiner does not consider a cited document to be sufficiently pertinent to use in a rejection, or otherwise does not consider it to be prior art for any reason, or even if the Examiner does not believe that the guidelines for citation have been fully complied with. This is requested so that each document becomes listed on the face of the patent issuing on the present application.

The present Disclosure Statement is being submitted in compliance with 37 CFR 1.56 insofar as an Examiner might consider any of the cited documents important in deciding whether to allow the application to issue as a patent, but the citation of each document is not to be construed as

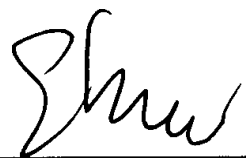
an admission that such document is necessarily relevant or prior art. No representation is intended that the cited documents represent the results of a complete search, and it is anticipated that the Examiner, in the normal course of examination, will make an independent search and will determine the best prior art consistent with 37 CFR 1.104(a) and 1.106(b) and, in the course of each search, will review for relevance every document cited on the attached form even if not initialed.

Early and favorable consideration is earnestly solicited.

Respectfully submitted,

Dated: _____

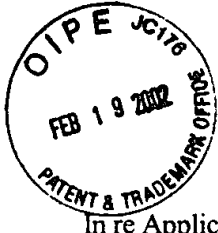
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 00-713-i16)

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In re Application of:

Chad A. Mirkin, et al.

Serial No. 09/976,601

Filed: October 12, 2001

For: Nanoparticles Having Oligonucleotides
Attached Thereto and Uses Therefor

Examiner: Jezia Riley

Art Unit: 1656

Confirmation No. 4367

RECEIVED

Commissioner for Patents and Trademarks
Washington, D.C. 20231

MAY 10 2002

FIFTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT **TECH CENTER 1600/2900**

Sir:

In order to comply with discretionary regulations 37 CFR §§1.97 and 1.98, attached hereto is Form PTO-1449, copies¹ of the documents listed thereon. These documents contain information which the Examiner may consider to be important in deciding whether to allow the present application to issue as a patent.

1. WO 92/04469 published 19 March 1992
2. WO 90/02205 published 8 March 1990

¹To the extent that a document is listed and no copy of same is attached, then such document is not at the present time available to the undersigned or is available in the file of a parent application. If a listed document is not in the English language and an English translation is readily available, such translation is also attached; if translation is not attached it is not readily available to the undersigned. If a foreign language patent document is cited, and an English language equivalent is known to the undersigned, then such equivalent patent is also cited on the attached form along with the corresponding foreign language patent and a connecting arrow indicated therebetween; if no such English language equivalent is cited, then none is known to undersigned.

3. Borman, *Chem.Eng. News*, December 9, 1996, pp. 42-43 (1996)

4. Tomlinson et al. *Anal Biochem*, Vol. 171, pp. 217-222 (1998)

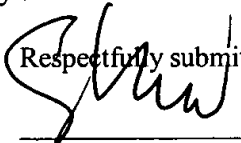
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Early and favorable consideration is earnestly solicited.

Dated: 1/31/02

Respectfully submitted,



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